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(21) International Application Number: PCT/EP95/04480 (22) International Filing Date: 14 November 1995 (14.11.95) (30) Priority Data: 08/339,985 14 November 1994 (14.11.94) US (71) Applicant (for all designated States except AT/DE): SANDOZ LTD. [CH/CH]; Lichtstrasse 35, CH-4002 Basle (CH). (71) Applicant (for DE only): SANDOZ-PATENT-GMBH [DE/DE]; Humboldtstrasse 3, D-79539 Lörrach (DE). (71) Applicants (for AT only): SANDOZ-ERFINDUNGEN VERWALTUNGSGESELLSCHAFT MBH [AT/AT]; Brunner Strasse 59, A-1230 Vienna (AT). SYSTEMIX, INC. [US/US]; 3155 Porter Drive, Palo Alto, CA 94304 (US). (72) Inventor: WICKREMA, Amittha; 842 Greennew Drive, Mountain View, CA 94040 (US). (74) Common Representative: SANDOZ LTD.; Patents & Trade-marks Div., Lichtstrasse 35, CH-4002 Basle (CH).		(81) Designated States: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT, UA, UG, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, LS, MW, SD, SZ, UG). Published <i>With international search report. Before the expiration of the time limits for amending the claims and to be republished in the event of the receipt of amendments.</i> (88) Date of publication of the international search report: 19 September 1996 (19.09.96)
(54) Title: ASSAY FOR THE MEASUREMENT OF MULTILINEAGE STEM CELLS AND METHODS OF USE THEREOF (57) Abstract <p>The present invention encompasses methods of detecting and quantitating hematopoietic stem cells in a population of hematopoietic cells. A population of hematopoietic cells is first obtained and treated to enrich for stem cells. Single cells in the enriched population are deposited onto a suitable growth substrate such as a well in a 96 well microtiter plate. The single cell deposits are cultured under conditions suitable to maintain viability and induce differentiation. The resultant populations are then assayed for the expression of lineage-specific messenger RNA transcripts specific to at least two different lineages. The presence of transcripts specific to two or more different lineages is scored as positive for the initial presence of a stem cell.</p>		

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INTERNATIONAL SEARCH REPORT

Int'l Application No
PCT/EP 95/04480

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12Q1/68 C12N5/08

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	WO,A,94 08039 (SYSTEMIX INC) 14 April 1994 see page 3, line 32 - line 34 see page 4, line 31 - page 5, line 15 see page 6, line 25 - line 30 see page 8, line 7 - page 9, line 3 see page 10, line 15 - page 16, line 27 ---	1-23,26 28
X	BLOOD. 83 (8). 1994. 2103-2114., XP000564654 THOMA S J ET AL 'Phenotype analysis of hematopoietic CD34+ cell populations derived from human umbilical cord blood using flow cytometry and cDNA-polymerase chain reaction'	1-23,25
Y	see the whole document ---	28
	-/--	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

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- *O* document referring to an oral disclosure, use, exhibition or other means
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T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

A document member of the same patent family

Date of the actual completion of the international search

30 May 1996

Date of mailing of the international search report

07.08.96

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 95/04480

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>BLOOD, FEB 1 1993, 81 (3) P647-55, UNITED STATES, XP000564653</p> <p>MOUTHON MA ET AL 'Expression of tal-1 and GATA-binding proteins during human hematopoiesis.'</p> <p>see the whole document</p> <p>-----</p>	1-23,27

INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP 95/ 04480

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. Claims 1-30: A method for detecting the presence of a hematopoietic stem cell
2. Claims 31-31: Oligonucleotides

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-30

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

Information on patent family members

PCT/EP 95/04480

Patent document
cited in search report

Publication date

Patent family member(s)

Publication
date

WO-A-9408039

14-04-94

AU-B-

5143393

26-04-94